GI

orthodromic primer and that described in SEQ ID NO.:4 as an antidromic primer. The sequences of SEQ ID NO.:3 and SEQ ID NO.:4 are those described in the above Nobuhara et al. nitride.--

Please replace the paragraph on page 14, lines 16-20 with the

following:

G2

--The product from the PCR method was separated by electrophoresis in 1.5% low-melting agarose (available from FMC) to cut out the DNA composed of about 360 bp corresponding to the amino acid sequence of SEQ ID NO.:2, which is defined as Fragment 1.

## **REMARKS**

Applicants submit herewith as Exhibit 1 a paper copy of a substitute sequence listing in response to the Examiner's Communication. Please replace the original sequence listing with the substitute sequence listing provided herewith.

The substitute sequence listing contains SEQ ID NOs: 1-4, wherein the original sequence presented at pages 20-21 of the application contains SEQ ID NOs: 1-3. SEQ ID NOs: 1, 3, and 4 of the substitute sequence listing correspond to SEQ ID NOs:1-3 respectively of the original sequence listing. SEQ ID NO:2 of the substitute sequence is automatically generated from SEQ ID NO:1 by the PatentIn program. As SEQ ID NO:2 contains as a separate sequence, the amino acid sequence shown in the original SEQ ID NO:1, no new matter is introduced by this substitute sequence listing. The amendments to the specification were simply made to indicate the appropriate SEQ ID NOs in the enclosed substitute sequence listing.

Also enclosed herewith are a computer diskette containing the substitute sequence listing (Exhibit 2) and a statement pursuant to 37 CFR §1.825(b)

stating that the computer diskette copy of the substitute sequence listing is identical to the paper copy (Exhibit 3).

Accordingly, no new matter is introduced by this amendment.

Finally, as required by 37 C.F.R. 1.121, a "marked up" version of the replacement paragraphs of the specification is attached as Exhibit 4 with additions indicated by underlining and deletions by brackets.

Respectfully submitted,
BIERMAN, MUSERLIAN AND LUCAS, L.L.P.

Date: Feb. 15, 2001

sy: dly m

Charles A. Muserlian Reg. No. 19,683

BIERMAN, MUSERLIAN AND LUCAS, L.L.P. 600 Third Avenue New York, NY 10016 (212) 661-8000 (212) 661-8002 Telecopier SEQUENCE LISTING

<110> SHIMURA, Takesada TORIYAMA, Satsuki

<120> CARTILAGE/ BONE INDUCING MATERIALS FOR REPARATION

<130> 146.1286

<140> 09/068,253

<141> 1998-06-09

<150> PCT/JP96/03333

<151> 1996-11-14

<150> JP 7/322402

<151> 1995-11-17

<160> 4

<170> PatentIn Ver. 2.1

<210> 1

<211> 357

<212> DNA

<213> Homo sapiens

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<221> CDS

<222> (1)..(357)

<223> Relevant amino acid residues in SEQ ID NO: 1 from 1 to 119 in WO 95/04819

<300>

<301> HOTTEN, Gertrud NEIDHARDT, Helge PAULISTA, Michael

<302> NEW GROWTH/DIFFERENT ATION FACTOR OF THE TGF-BETA

FAMILY

<310> WO 95/04819

<311> 1995-02-16

<313> 1 TO 119

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1

cgc (														7		96
gac (					_					_	_		/	_		144
ggg (						_	_			_		/	_			192
gca 9 Ala 1 65									_	-	/					240
ccc a										- 1						288
att (									•							336
gtg (			-		_			/	/							357
<210> 2																
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<212> PRT																
<213> Homo sapiens																
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Pro 1	Leu	Ala	Thr	Arg 5	Gln	Gly	Lys	Arg	Pro 10	Ser	Lys	Asn	Leu	Lys 15	Ala	
Arg	Cys	Ser	Arg 20	Lys	Ala	Leu	His	Val 25	Asn	Phe	Lys	Asp	Met 30	Gly	Trp	
Asp .	Asp	Trp 35	Ile	Ile	Ala	Pro	Leu 40	Glu	Tyr	Glu	Ala	Phe 45	His	Cys	Glu	
Gly	Leu 50	Cys	Glu	Phe	Pro	Leu 55	Arg	Ser	His	Leu	Glu 60	Pro	Thr	Asn	His	
Ala	Val	Ile	Gln	Thr	Leu	Met	Asn 2	Ser	Met	Asp	Pro	Glu	Ser	Thr	Pro	

```
65
                       70
                                            75
                                                                 80
 Pro Thr Cys Cys Val Pro Thr Arg Leu Ser Pro Ile Ser 1/1e Leu Phe
                   85
                                        90
                                                            95
 Ile Asp Ser Ala Asn Asn Val Val Tyr Lys Gln Tyr Gl/u Asp Met Val
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                                  105
                                                       110
 Val Glu Ser Cys Gly Cys Arg
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. <220>
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26

<400> 4

cgtcgactac ctgcagcca¢ acgact

Case No. <u>146</u>.1286

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):

SHIMURA, T. et al.

09/068,253

Group Unit: 1653

June 9, 1998

Examiner: Moezie, F.

CARTILAGE/ BONE INDUCING MATERIALS FOR

REPARATION

Statement Under 37 C.F.R. §1.821(f) or §1.825(b)

Commissioner of Patents Washington, D.C. 20231

Dear Sir:

I hereby certify that:

- The paper Sequence Listing submitted herewith and computer [] readable Sequence Listing attached hereto are identical (37 C.F.R. §1.821(f)).
- [X] The substitute paper Sequence Listing and substitute computer readable Sequence Listing submitted herewith are identical. No new matter is included (37 C.F.R. §1.825(b)).

Respectfully submitted,

BIERMAN, MUSERLIAN AND LUCAS, L.L.P.

Date: February 15, 2001

Charles A. Muserlian Reg. No. 19,683

BIERMAN, MUSERLIAN AND LUCAS, L.L.P. 600 Third Avenue, 28th Floor New York, NY 10016 (212) 661-8000 (212) 661-8002 Telecopier

## VERSION WITH MARKINGS TO SHOW CHANGES MADE

Please amend the paragraph on page 14, lines 3-7 as follows:

--Substitution was carried out according to the PCR method using an orthodromic PCR primer of SEQ ID NO.:[2]3. The DNA sequence of the PCR primer utilized the DNA described in SEQ ID NO.:[2]3 as an orthodromic primer and that described in SEQ ID NO.:[3]4 as an antidromic primer. [the sequence No. 2 and No. 3] The sequences of SEQ ID NO.:3 and SEQ ID NO.:4 are those described in the above Nobuhara et al. nitride.--

Please amend the paragraph on page 14, lines 16-20 as follows:

--The product from the PCR method was separated by electrophoresis in 1.5% low-melting agarose (available from FMC) to cut out the DNA composed of about 360 bp corresponding to the amino acid sequence of SEQ ID NO.:[1]2, which is defined as Fragment 1.--